REMARKS

This Amendment is in response to the Examiner's Office Action mailed on August 25, 03. Claims 1-42, 45 and 52-58 have been cancelled with prejudice. Claims 43 and 44 have been amended. Claims 43-44 and 46-51 are pending. Reconsideration is respectfully requested in view of the following remarks. For the Examiner's convenience and reference, Applicants' remakes are presented in the order in which the corresponding issued were raised in the Office Action.

I. Restriction as to Inventions

The Examiner has issued a restriction requirement stating that the application claims four separate inventions. Specifically, the Examiner identifies the four inventions as being:

Group I: Claims 52-56, drawn to a composition comprising a cytidine analog and imatinib mesylate;

Group II: Claims 1-30, 57 and 58, drawn to a method for treating chronic myelogenous leukemia (CML) with a DNA methylation inhibitor (cytidine analog);

Group III: Claims 31-42, drawn to a method for treating CML and decitabine such that the patient's resistance to imatinib mesylate in the absence of decitabine is reduced;

Group IV: Claims 43-51, drawn to a method for treating CML with a DNA methylation inhibitor in combination with imatinib mesylate.

Pursuant to 37 C.F.R. §1.142, Applicants elect Group IV without traverse and cancel without prejudice the claims of Groups I, II and III (Claims 1-42 and 52-58). Applicants reserve the right pursuant to 35 U.S.C. §121 to file one or more divisional applications directed to the non-elected inventions during the pendency of the present application.

II. Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 45 under 35 U.S.C. §112, Second Paragraph as being indefinite. Specifically, the Examiner states that the recitation of "determining a number of blasts....." in claim 45 failed to further limit the method of claim 44.

Applicants cancel claim 45 and amend claim 44 to specify that the patient is staged by determining a number of blasts, promyelocytes, basophil, or platelets per liter of peripheral blood or bone marrow. Withdrawal of the rejection under 35 U.S.C. §112, Second Paragraph is therefore respectfully requested.

III. Rejection under 35 U.S.C. §103(a)

The Examiner rejected claim 43-51 under 35 U.S.C. §103(a) as being unpatentable over Von Hoff et al. (Ann. Int. Med. 85(2) pp. 237-245, 1976) in view of Kantarjian et al. (Conference: Blood 98(11), part 1, pp 141a, 2001).

Specifically, the Examiner asserted that van Hoff et al. teach the use and effectiveness of 5-azacytidine in the treatment of acute myelogenous leukemeia; and Kantarjian et al. teach the treatment of CML with imatinib mesylate. The Examiner further asserted that "Kantarjian et al. also suggest a need for future clinical studies in CML treatment with imatinib mesylate in combination with decitabine (5-azacytidine)". Applicants respectfully traverse the Examiner's obviousness rejection based on the following reasons.

First, the Examiner errs in the assertion of decitabine being the same as 5-azacytidine. The correct chemical name of decitabine is 5-aza-2'-deoxycytidine. 5-azacytidine is another analog of cytidine.

Second, as acknowledged by the Examiner, von Hoff et al. do not provide specific disclosure where the patient's CML is staged prior to administration or the administration is performed when the patient is in blast phase of CML. Neither does the secondary reference, Kantarjian et al. Kantarjian et al. merely speculate that future clinical studies may be warranted for treating CML with a combination of imatinib mesylate and decitabine. Neither van Hoff et al. nor Kantarjian et al. teach or suggest the claimed method of treating a patient in blast phase of CML with a DNA methylation inhibitor (e.g., decitabine) at a dose ranging from 1 to 100 mg/m^2 per day in combination with imatinib mesylate.

In order to establish a 35 U.S.C. §103 rejection, an Examiner must produce the following enumerated elements to meet a minimum threshold for a *prima facie* case of obviousness. The Examiner must produce factual evidence of (i) a suggestion or motivation to combine or alter references; (ii) a reasonable expectation of success; and (iii) teaching or suggestion of all the claimed limitations. MPEP 2143. "If the examiner does not produce a *prima facie* case of obviousness, the applicant is under no obligation to submit evidence of non-obviousness." See MPEP 2142. Substantively, the Federal Circuit Court of Appeals has established that the nature and quality of the evidence of a suggestion or motivation to combine must be "clear and particular." *See Winner Intl' Royalty Corp. v. Wang,* 202 F.3d 1340, 1349 (2000). Moreover, the MPEP instruct that:

> Explicit finding on motivation or suggestion to select the claimed invention should also be articulated to support a 35 U.S.C. 103 ground for rejection. *Dillon,* 919 F.2d at 693, 16 USPQ2d at 1901; *In re Mills*, 916 F.2d 680, 683, 16 USPQ2d 1430, 1433 (Fed. Cir. 1990). Conclusory statements of similarity or motivation, without any articulated rationale or evidentiary support, do not constitute sufficient factual findings. (emphasis added). MPEP 2144.08 (III).

In this case, the Examiner's rejection under 35 U.S.C. §103 fails to establish the minimum threshold for an obviousness rejection. As discussed above, van Hoff et al. do not provide any suggestion or motivation for treating a patient in blast phase of CML with imatinib mesylate and 5-azacytidine at the specified dosage in independent claim 1. Kantarjian et al. merely suggest that imatinib mesylate and decitabine may be combined in the treatment of CML, but fail to provide any information as to the specific treatment regimen for such a combination therapy, let alone suggesting what type of CML patients should be treated. Thus, the cited references, individually or in combination, fail to teach or suggest the claimed combination therapy for a patient in blast phase of CML. Therefore, a prima facie case of obviousness under 35 U.S.C. §103 has not been established. Withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of the above amendment and remarks, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, Examiner is encouraged to telephone the undersigned.

The Commissioner is authorized to charge any additional fees that may be required, including petition fees, or credit any overpayment to Deposit Account No. 23-2415 (Attorney Docket No. 12636-260).

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